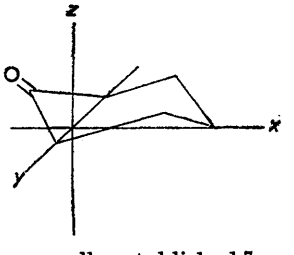
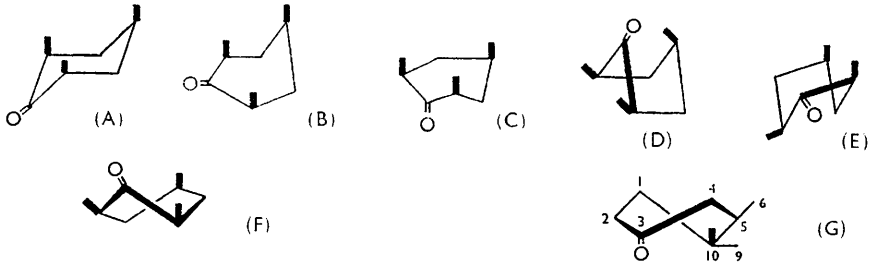
454. *Steroids. Part XXV.* The Stereochemistry of Ring A and the Nuclear Magnetic Resonance Spectra of Some Steroidal α-Halogenoketones*

By C. W. Shoppee, T. E. Bellas, Ruth E. Lack, and S. Sternhell

The n.m.r. spectra of 24 derivatives of 5α-cholestane with one carbonyl and one or more halogen functions in ring A are tabulated. The shielding of protons on carbon atoms adjacent to the carbonyl group and carrying a halogen substituent is discussed; the shape of the signals assigned to these protons is used to attribute " essentially axial " or " essentially equatorial " configurations to them. Long-range spin-spin coupling between protons on C-1 and C-3 in halogenated 5α-cholestan-2-ones is confined to the diequatorial pair. N.m.r. results indicate some deviation from the chair conformation of ring A in 2,2,4,4-tetrahalogeno-5α-cholestan-3-ones. Infrared, o.r.d., and n.m.r. evidence suggests that the chlorine atom in 2β-chloro-5α-cholestan-3-one has unexpectedly less axial character than the bromine atom in 2β-bromo-5α-cholestan-3-one.

The geometry of the regular chair conformation of cyclohexanone was investigated [1] by use of vector analysis; from the co-ordinates [1] we have calculated that the dihedral angle between the carbon–oxygen bond and the adjacent equatorial bonds is 15° 36′,[2] and that the inclinations of the adjacent axial bonds to the *xz*-plane and the *yz*-plane are +10° 32′ and +1° 29′, respectively. These angular parameters are altered by deviations from the regular chair conformation (A), such as the flattened chairs (B) and (C),[3,4] or by conversion into the alternative boats (D) and (E),[5] or the twisted boats (F),[6a] (" points " of the twist C-1, C-4) and (G) [6b] (" points " of the twist C-3, C-10). Such deviations resulting from steric crowding are well established,[7] and are reflected in ultraviolet, infrared, o.r.d., and n.m.r. spectra. Several studies have been reported [3,8,9] on the conformation of ring A





* Part XXIV, C. W. Shoppee, T. E. Bellas, R. E. Lack, and S. Sternhell, preceding Paper.

[1] E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, 1955, **77**, 2505.
[2] R. C. Cookson, *J.*, 1954, 282.
[3] N. L. Allinger and M. A. Da Rooge, *J. Amer. Chem. Soc.*, 1962, **84**, 4561.
[4] A. K. Bose, M. S. Manhas, and E. R. Malinowski, *J. Amer. Chem. Soc.*, 1963, **85**, 2795.
[5] C. W. Shoppee, *J.*, 1948, 1052.
[6] (*a*) W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Dreger, and W. N. Hubbard, *J. Amer. Chem. Soc.*, 1961, **83**, 606; E. W. Garbisch and D. B. Patterson, *ibid.*, 1963, **85**, 3228; (*b*) C. Djerassi and W. Klyne, *Proc. Nat. Acad. Sci. U.S.A.*, 1962, **48**, 1093.
[7] D. H. R. Barton and G. A. Morrison, *Fortschr. Chem. org. Naturstoffe*, 1961, **19**, 165.
[8] R. J. Abraham and J. S. E. Holker, *J.*, 1963, 806.
[9] A. Lablache-Combier, J. Levisalles, J. P. Pete, and H. Rudler, *Bull. Soc. chim. France*, 1963, 1689.

in heavily substituted steroids. In connexion with previous work [10-13] we had prepared 5α-cholestane derivatives with carbonyl and halogen functions in ring A. The present Paper deals with some spectroscopic properties of these compounds; the new spectroscopic data are in substantial agreement with values previously reported by us and by other workers.

Chemical Shifts of α-Protons in α-Halogenocyclohexanones.—Although axial protons generally [14,15] give rise to resonances upfield from those due to equatorial protons in the n.m.r. spectra of cyclohexane derivatives, it has recently been observed that a carbonyl group adjacent to a monohalogenated carbon atom in cyclohexanone [16] and some steroidal ketone derivatives [17] deshields the remaining α-proton when it is axial and shields it when it is equatorial. We have confirmed these observations by comparing the chemical shifts of 2α- and 2β-chloro-5α-cholestan-3-one, 2α- and 2β-bromo-5α-cholestan-3-one (Table 1), and 3α- and 3β-bromo-5α-cholestan-4-one (Table 2).[10,12] In the case of the epimeric 1α,3β-

TABLE 1

Nuclear magnetic resonance data on 5α-cholestan-3-one derivatives

	Chemical shift (τ)			
Compound	C-19 Me found	C-19 Me calc.*	Diff. (p.p.m.)	–CO–CH–Hal (H_2 and/or H_4)
5α-Cholestan-3-one.....	9·01	—	—	—
2β-Bromo-	8·79	8·76	−0·03	5·34 multiplet (cf. Figure a)
2α-Bromo-	8·91	8·93	+0·02	5·17 doublet of doublets, 13·4 and 6·5 c./sec.
2β-Chloro-	8·86	8·81	−0·05	5·65 doublet of doublets, 4·3 and 6·5 c./sec. (cf. Figure b)
2α-Chloro-	8·90	8·92	+0·02	5·40 doublet of doublets, 13·5 and 6·2 c./sec.
4α-Bromo-	8·92	8·93	+0·01	5·42 doublet ,12·2 c./sec.
2α,4α-Dibromo-	8·84	8·85	+0·01	H_2: 5·05 doublet of doublets, 6·2 and 13·6 c./sec.; H_4: 5·20 doublet, 12·7 c./sec.
2,2-Dichloro-	8·79	8·72	−0·07	—
2,2-Dibromo-	8·76	8·68	−0·08	—
2,2,4α-Trichloro-	8·70	8·63	−0·07	4·92, doublet 12·2 c./sec.
4α-Bromo-2,2-dichloro-...	8·75	8·64	−0·11	4·85, doublet 12·5 c./sec.
2,2,4α-Tribromo-	8·73	8·60	−0·13	4·80, doublet 12·5 c./sec.
4,4-Dibromo-2,2-dichloro-	8·67	8·39	−0·28	—
2,2,4,4-Tetrabromo-	8·63	8·35	−0·28	—

* Using the replacement values from ref. 37*a*.

TABLE 2

Nuclear magnetic resonance data on 3-halogeno-5α-cholestan-4-ones

	Chemical shift (τ)	
Compound	C-19 Methyl *	3-Proton
3α-Chloro-4-one †.....	9·26	5·82 (approximate triplet with spacings of 2·8 c./sec.)
3α-Bromo-	9·27	5·75 (doublet of doublets with spacings of 3·1 and 2·9 c./sec.)
3β-Bromo-	9·24	5·33 (doublet of doublets with spacings of 12·3 and 7·1 c./sec.)

* The chemical shift (R. F. Zurcher, *Helv. Chim. Acta*, 1961, **44**, 1380) of the C-19 methyl group in 5α-cholestan-4-one is τ 9·27. As expected,[37] adjacent α- or β-halogen substituents have little effect on the position of this resonance. † C. W. Shoppee and R. E. Lack, unpublished work.

dibromo- and 1α,3α-dibromo-5α-cholestan-2-ones (Table 3) the chemical shift difference between the axial proton at C-3 (τ 4·50) and the equatorial proton at C-3 in the epimers

[10] C. W. Shoppee and R. E. Lack, *J.*, 1961, 3271.
[11] C. W. Shoppee, R. E. Lack, and J. Scott, *J.*, 1962, 2233.
[12] C. W. Shoppee and T. E. Bellas, *J.*, 1963, 3366.
[13] C. W. Shoppee, F. P. Johnson, R. E. Lack, R. J. Rawson, and S. Sternhell, preceding Paper.
[14] R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Amer. Chem. Soc.*, 1957, **79**, 1005; 1960, **80**, 6098.
[15] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy to Organic Chemistry," Pergamon Press, 1959, ch. 6 and 7.
[16] K. M. Wellman and F. G. Bardwell, *Tetrahedron Letters*, 1963, 1703.
[17] A. Nickon, M. A. Castle, R. Harada, C. E. Berkoff, and R. O. Williams, *J. Amer. Chem. Soc.*, 1963, **85**, 2185.

TABLE 3

Nuclear magnetic resonance data on 5α-cholestan-2-one derivatives *

Compound	Chemical shift (τ) C-19 Me	1-Proton(s)	3-Proton(s)
5α-Cholestan-2-one ...	9·26	—	—
1α-Bromo-	9·11	5·92 †	—
3α-Bromo-	9·27	—	5·66, W_H = 5 c./sec.
3α-Chloro- §.....	9·09	—	5·83, W_H = 6 c./sec.
1α,3β-Dibromo-	9·08	5·70, $W_H - W_{H_{TMS}}$ = 0·3 c./sec.	4·50 ‡
1α,3α-Dibromo-	9·08	5·88, $W_H - W_{H_{TMS}}$ = 2 c./sec.	5·64, W_H = 7 c./sec.
1α,3,3-Tribromo-	9·10	5·69, $W_H - W_{H_{TMS}}$ = 0·7 c./sec.	—

* Signals assigned to H_1 and H_3 were unresolved multiplets (unless otherwise indicated). W_H denotes width at half height, $W_H - W_{H_{TMS}}$ denotes width at half height corrected for W_H of tetramethylsilane present as internal standard. † Doublet, splitting ≈1 c./sec. ‡ Doublet of doublets, splitting: 13 and 5 c./sec. § C. W. Shoppee and R. E. Lack, unpublished work.

(τ 5·64) is almost three times as large as that for the other epimeric pairs examined. Analogy with previously reported effects [18] strongly suggests that this is due to the presence of two 1,3-diaxial bromine atoms.

Configurational and Conformational Assignments from the Magnitude of Vicinal Coupling Constants.—The determination of exact values of dihedral angles from the magnitudes of the vicinal coupling constants is not reliable [19] because of the influence of factors other than geometrical ones, such as the polar character [20,21] and configuration [22] of substituents and possibly also of other, still undetermined factors.[23] However, the assignment of signals to " essentially axial " or " essentially equatorial " protons in six-membered rings on the basis of the approximate magnitudes of vicinal coupling constants, or of the width of multiplets at half-heights,[24] remains, so far, unchallenged.

In the compounds investigated here, the signals due to protons on carbon atoms adjacent to a carbonyl group and also carrying a halogen substituent could always be identified (Tables 1—3) as those occurring at the lowest field. Where this signal was a multiplet with splitting larger than 10 c./sec., the proton concerned was assigned an " essentially axial " configuration, and where it was a multiplet with the largest splitting not exceeding 7 c./sec. or with a width at half-height not exceeding 15 c./sec., it was assigned an " essentially equatorial " configuration. The configurations thus assigned confirm those arrived at previously on other grounds.[10-13]

Long-range Spin–spin Coupling in 5α-Cholestan-2-one Derivatives.—Table 3 shows that the signals due to the 1β-protons in 1α-bromo-5α-cholestan-2-one and 1α,3α-dibromo-5α-cholestan-2-one are split or appreciably broadened whilst the 1β-protons in 1α,3β-dibromo-5α-cholestan-2-one and 1α,3,3-tribromo-5α-cholestan-2-one give rise to narrow singlets. We interpret this result as showing that appreciable long-range spin–spin coupling in the system *H*–C–CO–C–*H* in ring A is confined to the pair of equatorial protons on C-1 and C-3. This is in accord with the steric requirements for effective long-range coupling which have been proposed [25,26] for the system *H*–C–CO–C–*H* [27] in general, and

[18] M. Tomoeda, M. Inuzuka, T. Furuta, and T. Takahashi, *Tetrahedron Letters*, 1964, 1233, and refs. therein.
[19] M. Karplus, *J. Amer. Chem. Soc.*, 1963, **85**, 2870.
[20] K. L. Williamson, *J. Amer. Chem. Soc.*, 1963, **85**, 516.
[21] K. L. Williamson, C. A. Lanford, and C. R. Nicholson, *J. Amer. Chem. Soc.*, 1964, **86**, 762.
[22] D. H. Williams and N. S. Bhacca, *J. Amer. Chem. Soc.*, 1964, **86**, 2742.
[23] A. C. Huitric, J. B. Carr, W. F. Trager, and B. J. Nist, *Tetrahedron*, 1963, **19**, 2145.
[24] A. Hassner and C. Heathcock, *J. Org. Chem.*, 1964, **29**, 1350.
[25] E. W. Garbisch, Abstracts 145th National Meeting, Amer. Chem. Soc., Sept. 1963, 36Q, and personal communications.
[26] A. Rassat, C. W. Jefford, L. M. Lehn, and B. Waegell, *Tetrahedron Letters*, 1964, 233.
[27] S. Sternhell, *Rev. Pure and Appl. Chem.*, 1964, **14**, 15.

which are the same as those governing similar long-range coupling in completely saturated systems (the so called " M," " W," or " tail-to-tail " rule).[26-32]

Maximum long-range coupling is associated with a planar structure, and this has been interpreted [25] as evidence that the interaction is transmitted through σ-bonds only rather than through a mechanism involving π-electrons.[33] However, the much smaller spin–spin coupling formally across the same bond system *H*–C–CO–C–*H* in non-cyclic systems [27,33-35] may well involve an alternative spin–spin coupling mechanism.[27,36]

Conformation of Ring A in α-Halogenated 5α-Cholestan-3-ones.—We have examined the n.m.r. spectra (Table 1) of some 5α-cholestan-3-one derivatives halogenated at C-2 and/or at C-4, to obtain evidence about the conformation of ring A, particularly in the case of 2,2,4,4-tetrahalogeno-derivatives where severe 1,3-diaxial interactions must occur.

Malinowski *et al.*[37a] and Zurcher [37b] have described the effect of symmetry on the chemical shift of C-19 methyl groups in steroids and noted the equivalence of positions 2, 4, and 6 in a *trans*-A/B-steroid existing in the all-chair conformation. Table 1 compares the chemical shifts of the C-19 methyl groups with those calculated by use of the replacement constants of Malinowski *et al.*,[37a] with the further assumption that 4β-halogen substituents should have the same effect as the corresponding 2β- and 6β-substituents. It can be seen that, while agreement between the experimental and calculated values for the dihalogenated derivatives is reasonable, a marked deviation occurs with the more highly substituted compounds, especially in the case of the 2,2,4,4-tetrahalogeno-derivatives where the difference between the calculated and experimental figure is 0·28 p.p.m. We consider that these results indicate a departure from the regular chair conformation (A) of ring A with the consequent breakdown of additivity rules for the chemical shifts of C-19 methyl groups.[32] It is interesting to note that while the calculated and experimental values for the chemical shifts of the C-19 methyl group in 4α-bromo-2,2-dichloro-5α-cholestan-3-one and 2,2,4α-tribromo-5α-cholestan-3-one appear to deviate significantly (0·11 and 0·13 p.p.m.), the 4-protons in both compounds give rise to doublets with a separation of 12·5 c./sec., showing that they are essentially axial (see above). This may indicate either that the distortion occurring is of such a nature (C) as to leave the conformation at C-4 and C-5 unaltered from that assumed when ring A is a regular chair form, or that the chemical shifts of C-19 methyl groups are substantially more sensitive to changes in conformation than vicinal coupling constants.*

The chemical shifts and shapes of the signals assigned to protons on C-2 and C-4 in the remaining compounds in this series (Table 1) give no indication (see above) of any substantial deviation from the regular chair conformation. In the n.m.r. spectra of all 2,2-dihalogeno-derivatives (whether further halogenated at C-4 or not), the methylene protons at C-1 gave rise to an easily identified AB quartet (Table 4) which could be analysed according to standard procedure,[38] although in some cases the upfield half was partially overlapped by other resonances. On general grounds [14,15] it is likely that the downfield

* A Referee suggested that the non-additivity of methyl shifts in the polyhalogenated derivatives may be due to causes other than purely steric distortion, and in particular to hindered rotation [37b] of the C-19 methyl group.

[28] D. Gagnaire and E. Payo-Subiza, *Bull. Soc. chim. France*, 1963, 2627.
[29] E. I. Snyder and B. Franzus, *J. Amer. Chem. Soc.*, 1964, **86**, 1166.
[30] P. Laszlo and P. R. Schleyer, *J. Amer. Chem. Soc.*, 1964, **86**, 1171.
[31] (*a*) B. Waegell and C. W. Jefford, *Bull. Soc. chim. France*, 1964, 844; (*b*) B. Waegell, *ibid.*, p. 855.
[32] C. W. Shoppee, G. A. R. Johnson, R. E. Lack, and S. Sternhell, *Tetrahedron Letters*, 1964, 2319, and refs. therein.
[33] J. R. Holmes and D. Kivelson, *J. Amer. Chem. Soc.*, 1961, **83**, 2959.
[34] G. M. Whitesides and J. D. Roberts, *J. Phys. Chem.*, 1964, **68**, 1583.
[35] T. Takahashi, *Bull. Chem. Soc. Japan*, 1964, **37**, 291, 963.
[36] C. N. Banwell and N. Sheppard, *Discuss. Faraday Soc.*, 1963, No. 34, 115, and N. Sheppard, personal communication.
[37] (*a*) E. R. Malinowski, M. S. Manhas, G. H. Muller, and A. K. Bose, *Tetrahedron Letters*, 1963, 1161; (*b*) R. F. Zurcher, *Helv. Chim. Acta*, 1963, **46**, 2054.
[38] H. Rottendorf and S. Sternhell, *Tetrahedron Letters*, 1963, 1289.

(H_A) signals are due to the equatorial (or essentially equatorial) 1β-protons while the upfield (H_B) signals are due to the axial (or essentially axial) 1α-protons. Possible support for this assignment arises from the asymmetry observable in some of the AB quartets [27,38,39] (Table 4), which we ascribe to the effects of stereospecific long-range coupling with the C-19 methyl group.[32]

TABLE 4

AB-Spectra due to C-1 methylene protons

Compound	J_{AB} (c./sec.)	τ_A	τ_B
2,2-Dibromo-5α-cholestan-3-one	16	6·73	7·24
2,2,4α-Tribromo-5α-cholestan-3-one	16	6·72	7·23
2,2,4,4-Tetrabromo-5α-cholestan-3-one	17	6·57	6·91
2,2-Dichloro-5α-cholestan-3-one	15	6·95	7·69
4α-Bromo-2,2-dichloro-5α-cholestan-3-one *	15·5	6·91	7·63
2,2,4α-Trichloro-5α-cholestan-3-one	15	6·90	7·67
4,4-Dibromo-2,2-dichloro-5α-cholestan-3-one *	16	6·92	7·23

* The upfield half of the AB quartet is broader than the downfield part.

Assuming that the above assignments are correct, the following observations can be made and rationalised. The chemical shift of H_B in 2,2-dichloro-5α-cholestan-3-one is unaffected by the introduction of a 4α-chloro- or 4α-bromo-substituent but is shifted by 0·46 p.p.m. on the further introduction of a 4β-bromo-substituent. The chemical shifts due to H_A in the series are virtually unchanged. In the regular chair form of ring A, the axial 1α-proton and the 4β-bromine atom are not orientated in a manner likely to cause long-range shielding effects,[18] so that the large chemical shift produced by the introduction of a 4β-bromine atom can be attributed to a change in conformation of ring A (B, C). Similarly, the chemical shift of H_B in 2,2-dibromo-5α-cholestan-3-one (Table 4) is also unaffected by the introduction of a 4α-bromo-substituent, but the further introduction of a 4β-bromo-substituent causes, not only a substantial (0·32 p.p.m.) shift in the signal assigned to H_B, but also a smaller (0·15 p.p.m.) shift in the H_A resonance. This difference in behaviour between the 2,2,4,4-tetrabromo-5α-cholestan-3-one and 4,4-dibromo-2,2-dichloro-5α-cholestan-3-one may be rationalised by postulating a greater deviation from the regular chair form (A) in the former case, presumably owing to the larger van der Waals radii of the bromine atoms.

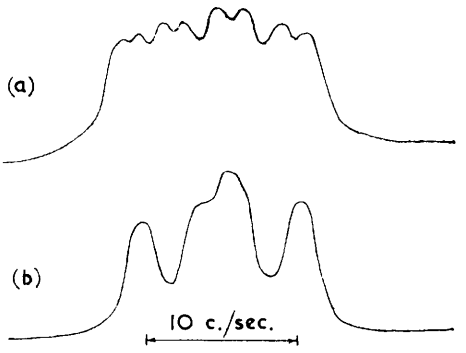
Conformation of 2β-Chloro-5α-cholestan-3-one and 2β-Bromo-5α-cholestan-3-one.—The n.m.r. data (Table 1) indicate that in 2β-chloro-5α-cholestan-3-one and 2β-bromo-5α-cholestan-3-one the halogen atoms are essentially axial. Thus, in both cases the signals due to the C-19 methyl groups appear significantly downfield from that in the parent 5α-cholestan-3-one,[37a] and the 2α-protons give rise to signals whose shape and position (with respect to those of the 2β-protons of the corresponding epimeric 2α-halogeno-derivatives) show them to be essentially equatorial (see above). However, while the signal due to the 2α-proton in 2β-bromo-5α-cholestan-3-one (Figure a) shows additional fine structure expected (see above) from an equatorial–equatorial long-range coupling with the 4α-equatorial proton, the signal due to the 2α-proton in 2β-chloro-5α-cholestan-3-one (Figure b) shows no evidence of additional splitting.[40] We interpret this result as indicating that, whilst in both halogeno-ketones the halogen atoms are essentially axial, the chlorine atom in 2β-chloro-5α-cholestan-3-one deviates more from the regular axial conformation (A) than the bromine atom in 2β-bromo-5α-cholestan-3-one.

This interpretation is supported by o.r.d. measurements in which the contribution Δa of the 2β-chlorine atom in 2β-chloro-5α-cholestan-3-one is +38 compared with +65 for the contribution of the 2β-bromine atom in the corresponding 2β-bromo-ketone.[41] The

[39] R. M. Carman and N. Dennis, *Austral. J. Chem.*, 1964, **17**, 395.
[40] E. W. Garbisch, *J. Amer. Chem. Soc.*, 1964, **86**, 1780.
[41] W. Klyne and C. Djerassi, *J.*, 1963, 2390.

somewhat lower figure in the former case is probably due to greater distortion [42] of ring A in 2β-chloro-5α-cholestan-3-one.

The infrared spectrum of 2β-bromo-5α-cholestan-3-one shows the carbonyl stretching band at 1722 cm.$^{-1}$ in Nujol and in potassium bromide discs, and at 1719 in carbon tetrachloride (cf. 1714 cm.$^{-1}$ for 5α-cholestan-3-one). 2β-Chloro-5α-cholestan-3-one shows the carbonyl maximum at 1721 cm.$^{-1}$ (in carbon tetrachloride), but in the solid state (in Nujol and in potassium bromide discs) the spectrum shows two carbonyl bands at 1735 (chlorine equatorial) and 1718 cm.$^{-1}$ (chlorine axial), the former being slightly more intense. After immersion of a potassium bromide disc in carbon tetrachloride, the dissolved chloro-ketone exhibited the carbonyl maximum as a single peak at 1721 cm.$^{-1}$. These infrared data can be interpreted as disclosing some distortion of ring A in both halogeno-ketones in solution, whilst in the solid state the crystal-lattice forces in 2β-chloro-5α-cholestan-3-one are



Portions of n.m.r. spectra of (a) 2β-bromo-5α-cholestan-3-one, and (b) 2β-chloro-5α-cholestan-3-one, showing the signals assigned to protons on C-1. The chemical shifts are recorded in Table 1. The spectra here reproduced were obtained with the aid of an electronic timing device for improving the signal to noise ratio, designed and operated by Mr. Carl Dehlsen

sufficient to convert the distorted chair form of ring A partially into the boat conformation (D) in which the 2β-chlorine atom is equatorial. There appears to be no information concerning the influence of α-halogen substituents in the alternative boat conformation (E), in which the 2β-halogen atom would possess a " bowsprit " orientation, on o.r.d. or infrared spectra; however, this conformation for a 5α-cholestan-3-one seems improbable because of the 2αH,5αH-interaction.

The conformation of 2-bromocyclohexanone and 2-chlorocyclohexanone in various solvents has been studied by means of dipole moments [43] and n.m.r.[40,44] It is clear that the combination of factors [43] is such that bromine has a greater preference for the axial conformation than has chlorine.* In the case of the 2β-halogeno-5α-cholestan-3-ones, an additional factor would be the 1,3-diaxial interaction between the essentially axial 2β-halogen atom and the C-19 methyl group, which would be expected to be more severe for bromine than for chlorine. In spite of this, the balance of factors appears to be such as to favour the axial conformation of bromine in 2β-bromo-5α-cholestan-3-one to a larger extent than the axial conformation of chlorine in 2β-chloro-5α-cholestan-3-one.

It is interesting to note that in 2β-fluoro-5α-androstane-3,11-dione [45] there is no evidence of any distortion of the regular chair conformation of ring A. Work on the preparation of the corresponding iodo-compounds is in progress in these laboratories.

The Chemical Shifts of the C-18 *Methyl Group.*—In all compounds examined the signal assigned to C-18 methyl group was found between τ 9·32 and 9·35.

* N.m.r. studies on 2-chlorocyclohexanone show that the chlorine atom has substantially less preference for the axial conformation than the bromine atom in 2-bromocyclohexanone.[44]

[42] W. Klyne, personal communication.
[43] N. L. Allinger, J. Allinger, L. A. Freiberg, R. F. Czaja, and N. A. Le Bel *J. Amer. Chem. Soc.*, 1960, **82**, 5876, and refs. therein.
[44] R. J. W. Le Fèvre and C. Y. Chen, personal communication.
[45] N. L. Allinger M. A. Da Rooge, M. A. Miller, and B. Waegell, *J. Org. Chem.*, 1963, **28**, 780.

Experimental

For general directions see *J.*, 1959, 345. Infrared spectra were determined in a Perkin-Elmer model 221 double-beam instrument. N.m.r. spectra were determined on a Varian A 60 instrument at 60 Mc./sec., in deuteriochloroform with tetramethylsilane as internal reference.

In the n.m.r. spectra, the calibration of the sweep was checked with the position of the chloroform signal (isotopic impurity in solvent) which was always found within 434—436 c./sec. downfield from the signal due to tetramethylsilane. The position of the resonances of the solutes was independent of the concentration (dilute solution of tetramethylsilane and chloroform in carbon tetrachloride) in several instances when a check was made. The linearity of the sweep was checked with a frequency counter. Most of the measurements were made at least in duplicate; deviations were within the accuracy of reading the spectra (±1 c./sec.).

In spite of the reproducibility and lack of concentration dependence in a number of instances where literature values were available,[8,17] discrepancies of the order of 0·05—0·10 p.p.m. became apparent for spectra obtained with the same model instrument. While these discrepancies are too small to lead to any ambiguity in the interpretation, they underline the fact that extreme care must be taken in all arguments based on small difference in chemical shifts.

2β-*Chloro*-5α-*cholestan*-3-*one*.—Optical rotatory dispersion: in MeOH, [*M*] +5340° (324 mμ, peak), −3950° (267 mμ, trough).

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